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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,868	10/24/2001	Rifat Pamukcu	P-168-1	8300

7590 12/19/2002  
Cell Pathways, Inc.  
702 Electronic Drive  
Horsham, PA 19044

EXAMINER

OWENS JR, HOWARD V

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 12/19/2002

4

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/003,868

Applicant(s)

PAMUKCU ET AL.

Examiner

Howard V Owens

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

#### **Claim Objections**

In claims 2, 4 and 6 the terms "5 to 6membered" a space should be rendered between 6 and membered.

#### **Claim Rejections - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, use of the term "general" implies that the compound is not confined by specialization to the claimed structure or substituents thereof. As claimed, the benzimidazole derivative is selected from the specific substituents and core structures set forth in the instant application, these core structures and substituents can not be general in structure or substituents, but must be specific or defined to that which is claimed. Accordingly, dependent claim 2 is rejected as well as it fails to obviate the rejection set forth in the parent claim.

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In claims 1 and 5, the variable "B" in the formula "-B-R<sup>4</sup>" is not defined in the instant claim.

In claim 1, the placement of a period after the terms "a pyrrolylcarbonyl group" renders the claim vague and indefinite as to whether applicant intends the claim to be terminated.

Claims 1-6 contain one or more parenthetical phrases, creating embedded text, which renders the claims in which they appear in all occurrences indefinite because it is unclear whether the limitations in the parenthetical phrases are part of the claimed invention. Removal of the parentheses and the incorporation of the text of said phrases syntactically into the claims would obviate this rejection.

Any claims which depend from the indefinite claims rejected above that fail to remedy said rejection(s), are also deemed to be indefinite.

### **35 U.S.C. § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains: Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishi et al., U.S. Patent No. 5,998,437 in combination with Taylor et al., U.S. Patent No. 4,950,680, Earnest et al., Journal of Cellular Biochemistry, supplement 161:pp. 156-166 and Fang et al., Journal of Biological Chemistry, vol.272(23), pp. 14860-14866.

Claims 1-6 are drawn to a method of treating a mammal having a precancerous lesion, inhibiting neoplastic cells and regulating apoptosis comprising administering a pharmacologically effective amount of a fused pyrimidine compound of formula 1.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Nishi et al. teach fused pyridine inhibitors analogous to those set forth in the instant claims (see abstract and columns 2-16) and teach that these derivatives are selective inhibitors of cGMP phosphodiesterase (col. 1, line 41 - col.2, line 14). However, Nishi does not teach the treatment of precancerous lesions, the inhibition of neoplastic cells nor the regulation of apoptosis as uses for the compounds.

Fang et al. teach that a cGMP-phosphodiesterase inhibitor can induce apoptosis in cardiac myocytes (p. 14863) which adequately bridges the nexus between the use of compounds which have an inhibitory effect on cGMP-PDE as inducers of apoptosis.

Taylor et al. teach (col.3, line 43 - col. 4, line 55 and col. 5, lines 15-20) that tumor metastasis is enhanced by tumor cell interactions with platelets and that agents which block or prevent tumor cell-platelet interaction and aggregation such as inhibitors of TXA<sub>2</sub> synthetase and phosphodiesterase have antimetastatic effects; moreover, Earnest et al. teach that phosphodiesterases and cyclic cGMP kinases (and inhibitors thereof) may be central to cancer initiation and promotion (see abstract and pp. 157-159) which adequately bridges the nexus between the differences in the prior art and the invention as claimed.

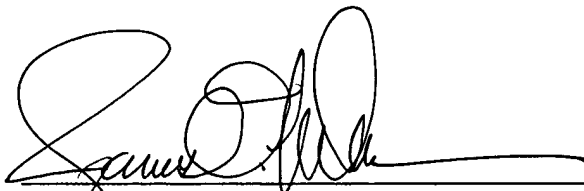
It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use a fused pyrimidine of formula I to treat precancerous lesions, inhibit neoplastic cells or regulate apoptosis.

A person of ordinary skill in the art would have been motivated to use the fused pyrimidines of formula I to treat precancerous lesions, inhibit neoplastic cells or regulate apoptosis as the prior art teaches that these compounds as inhibitors of TXA<sub>2</sub> synthetase and phosphodiesterase have an anti metastatic effect through the inhibition of tumor cell induced platelet aggregation. The test for obviousness is not whether the

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features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). One of skill in the art would have a reasonable expectation of success in the treatment of precancerous lesions with the fused pyrimidine compounds of the invention, or any compound for that matter which inhibits cGMP phosphodiesterase as the inhibition of this enzyme has been shown in the prior art to disrupt the cellular cascade from which certain neoplasms are formed.

Howard V. Owens  
Patent Examiner  
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A handwritten signature in black ink, appearing to read 'James O. Wilson', written over a horizontal line.

James O. Wilson  
Supervisory Patent Examiner  
Technology Center 1600

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Supervisory Patent Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.